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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/613,975	07/03/2003	Donald L. Wise	CSI 130	8618

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EXAMINER	
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ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 08/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/613,975	WISE ET AL.	
	Examiner	Art Unit	
	Khatol S. Shahnan-Shah	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicants' petition to revive the application, notice of appeal and appeal brief received February 22, 2006 are acknowledged.

2. In view of the appeal brief filed on February 22, 2006, PROSECUTION IS HEREBY REOPENED. New rejections are set forth below. To avoid abandonment of the application, appellant must exercise one of the following two options: (1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or, (2) initiate a new appeal by filing a notice of appeal under 37 CFR 41.31 followed by an appeal brief under 37 CFR 41.37. The previously paid notice of appeal fee and appeal brief fee can be applied to the new appeal. If, however, the appeal fees set forth in 37 CFR 41.20 have been increased since they were previously paid, then appellant must pay the difference between the increased fees and the amount previously paid. A Supervisory Patent Examiner (SPE) has approved of reopening prosecution by signing below:

Status of Claims

3. Claims 1, 3-11 are pending in this application.

Note: Applicants in the Appeal brief page 2 recite status of claims as claims 1 and 3-11 as pending. Claims 12-21 and **3** have been canceled. It looks like as the applicants have made a typographical error in regard to canceled claims. According to the record claim **2** has been canceled, not claim **3**.

Rejections Withdrawn

4. Rejection of claims 1-11 under 35 U.S.C. 112 first paragraph made in paragraph 9 of the office action mailed December 22, 2003 is withdrawn. New rejections are set forth below.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1, 3-11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition (a mucoadhesive controlled released particulate delivery system) inducing immunogenic response against certain pathogens (Malaria and Anthrax), does not reasonably provide enablement for a vaccine for inducing immune response against all pathogens as claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP) 2164.01(a). Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples (6) the quantity of experimentation, (7) the relative skill of those in the art, and (8) the breadth of the claims.

In the instant case claims 1, 3-11 are very broad and drawn to a vaccine. The only given example in the specification is in pages 11 and 14, mentioning the production of antigens for certain species of malaria and anthrax. When a compound or composition claim is limited by a particular use, enablement of that claim should be evaluated base on that limitation. See in re Vaeck, 947 F. 2d 488, 495,20 USPQ 2d 1438, 1444 (Fed Cir, 1991).

Dorland's Medical Dictionary (29th Edition, 2000) defines "vaccine" as "a suspension of attenuated or killed microorganisms (bacteria, viruses, or rickettsiae), or of

antigenic proteins derived from them, administered for the **prevention, amelioration, or treatment of infectious diseases**. In the instant case the applicants' invention is not enabled for the **prevention, amelioration, or treatment of all infectious diseases**. And one skilled in the art will not be able to make/and or use the invention without undue experimentation commensurate in scope with the claims.

Stedman's Medical Dictionary (27th Edition, 2000) defines pathogen any virus, microorganism (i.e. bacteria, parasites and fungi) or other substance causing disease. The term pathogen is very broad and can include any organism or substance disease causing in humans, animals, plants, fish etc.

The term inducing immune response is also broad and include preventive immune response, as well induced and innate immune response.

Applicants argue (page 4 of appeal brief) that the invention relates to the development of effective and long lasting vaccines incorporating nucleic acid encoding antigen, such as plasmid DNA, by encapsulating the DNA with a mucoadhesive controlled released particulate formulation. In page 5 of the appeal brief applicants argue the they are not claiming any unique DNA, merely DNA encoding antigens that are present in the pathogens. Applicants further argue that vaccines, including DNA vaccines, have been widely available for a long time. The invention here is to put them into a mucoadhesive controlled release particulate formulation. Applicants' arguments have been fully considered but they are not persuasive because the specification, while being enabling for a mucoadhesive controlled released particulate delivery system) inducing immunogenic response against certain pathogens (Malaria and Anthrax) does not reasonably provide enablement for a vaccine for inducing immune response against all pathogens. The claims are very broad and drawn to a vaccine, which encompasses any pathogen. The specification fails to teach a skilled artisan how to administer the claimed composition for immune protection. The specification presents a paper protocol in this regard. The specification has not taught a skilled artisan how to use the invention as presently claimed. Applicants have not shown or disclosed a correlation between in vitro and in vivo studies or that there are animal models that correlate to human (i.e. person) efficacy. Applicants' specification fails to provide guidance to the

skilled artisan on the parameters for DNA vaccine for the breadth of the claimed invention. Numerous factors complicate the DNA vaccine therapy art, which have not been shown to be overcome by routine experimentation. These include, the fate of the DNA vector itself (volume of distribution, rate of clearance into the tissues, etc.), the *in vivo* consequences of altered gene expression and protein function, the fraction of vector taken up by the target cell population, the trafficking of the genetic material within cellular organelles, the rate of degradation of the DNA, the level of mRNA produced, the stability of the mRNA produced, the amount and stability of the protein produced, and the protein's compartmentalization within the cell, or its secretory fate, once produced. These factors differ dramatically based on the vector used, the protein being produced, and the disease being treated. Attwood, T. K. (Science Vol. 290,) October 20, 2000) teach that to predict genes in uncharacterized DNA is unreliable, it is presumptuous to make functional assignments merely on the basis of some degree of similarity between sequences, and knowing the structure does not inherently tell us the function (see page 471). In the instant invention there is no correlation between structure and function. Additionally, the specification does not provide any working examples, which enable the claimed invention. Nor does the specification provide any guidance to the skilled artisan on how to make and use genetic (i.e. DNA) constructs of all pathogens, which would result in the desired effect (prevention and treating disease). Even assuming that an effective genetic material is constructed, it is not evident that DNA encode specific antigen to elicit immune response or to prevent disease. Therefore, even if the specification enabled the construction of the delivery vehicle comprising malaria DNA in mice, in the absence of particular guidance, the artisan would have been required to develop *in vivo* and *ex vivo* means of practicing the claimed methods and such development in the nascent and unpredictable DNA vaccine art would have been considered to have necessitated undue experimentation on the part of the practitioner.

A disclosure in an application, to be complete, must contain such description and details as to enable any person skilled in the art or science to which it pertains to make and use the invention as of its filing date, In re Glass, 181 USPQ 31; 492 F2.d 1228 (CCPA 1974). While the prior art setting may be mentioned in general terms, the

essential novelty, the essence of the invention, must be described in such details, including proportions and techniques where necessary, as to enable those persons skilled in the art to make and utilize the invention. For example applicants argue that prior art shows that DNA vaccines are considered to be enabled and as evidence give reference to Pachuk et al. (Current Opinion in Molecular Therapy Vol. 2, No. 2, 2000, prior art of record, applicants' Form 1449). It is the examiner's position that the same reference, page 188 recites " DNA vaccine technology, however, is still in its infancy and much research needs to be done to improve the efficiency with which these vaccines work with humans" page 195 under conclusion the paper recites " It is recognized that one of the major limitations to the success of DNA vaccines is its delivery", (see Pachuk et al. page 195). Pachuk et al. recite that structure rational designs for DNA delivery are limited. In addition it is unclear as to which cell type should be targeted for DNA delivery for optimal elicitation of immune response (see page 188 right column, 2nd paragraph). McDonnel et al. of University of Michigan (Medscape General Medicine, Vol.1, No 3, 1999) summarize problems with DNA vaccines as following: There are many problems and unanswered questions concerning the use of DNA vaccines. The possibility of insertional mutagenesis is a concern that needs to more rigorously tested. While there is no evidence that the introduced DNA integrates into the host genome, if it were to occur, it would raise the specter of carcinogenesis; oncogensis may be turned on or tumor suppressor genes inhibited. What if DNA circulated throughout the body after delivery? Might subsequent generation express the antigen from birth and develop tolerance instead of immunity to the pathogen? Anti-DNA antibody formation and the possibility of autoimmune disease is another concern (see page 4 of 6 The emerging Role of DNA Vaccines, Medscape). In conclusion the specification does not support the broad scope of the claims, which encompass recombinant forms and any isolated phages. Thus, applicant has **not** provided sufficient guidance to enable one of ordinary skill in the art to how to make and use the claimed invention in manner reasonably correlated with the scope of the broad claims.

In view of all of the above, in view of the lack of predictability in the art, it is determined that it would require undue experimentation to make and use the

Invention commensurate in scope with the claims.

7. Claims 1, 3-11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a written description rejection.**

Claims 1, 3-11 are drawn to vaccine composition for inducing immune response to a pathogen.

The specification and the claims do not indicate what distinguishing attributes are shared by the members of the genus (Pathogens). Thus the scope of the claims include numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. Since the disclosure fails to describe the common attributes or characteristics that identify the members of the genus, and because the genus is highly variant, and since there is no sequence information has been given for any of these claimed DNA for all pathogens. There is an inverse correlation between the level of predictability in the art and the amount of disclosure necessary to satisfy the written description requirement. For example there is a well- established correlation between structure and function in the art. But in the instant invention the specification does not describe a structure or a function for the claimed species. There is insufficient written description in the specification to describe the genus of pathogens recited. Thus applicant has not described a function or a structure, which is shared by the genomic DNA of the pathogens, which would adequately describe the genus. The applicants have only described delivery of DNA of malaria parasite in mice (page 32). Even the given example does not provide enough guidance to how the DNA for delivery was selected. One skilled in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus of the variants. For example Attwood, T. K. (Science Vol. 290, October 20, 2000) teach that to predict genes in uncharacterized DNA is unreliable, it is presumptuous to make functional assignments merely on the basis of some degree of similarity between sequences, and knowing the

structure does not inherently tell us the function (see page 471). In the instant invention there is no correlation between structure and function. There are no working examples how to make a DNA from other genus and species of the pathogens. There is no sequence information recited in the specification encompassing DNA of any other pathogens. Thus applicant was not in possession of the claimed genus.

Adequate written description requires more than a mere statement that is part of the invention and a reference to a potential method of isolating it. The structure itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. LTS.* 18 USPQ 2d 1016. Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Application Under 35 U.S.C. 112, 1 "Written Description" Requirement, Federal Register, Vol. 64, No.244, pages 71427-71440, Tuesday December 21, 1999.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

9. Claim 9 is indefinite by reciting improper Markush language. Alternative expressions are permitted if they present no uncertainty or ambiguity with respect to the question of scope or clarity of the claims. One acceptable form of alternative expression, which is commonly referred to as a Markush group, recites members as being "selected from the group consisting of A, B and C." See Ex parte Markush, 1925 C.d. 126 (Comm'r Pat. 1925). Claim 9 recites wherein the pathogen is selected from the group consisting of malaria, tularemia, anthrax and Helicobacter pylori. In the recited group Helicobacter pylori is only a pathogen and The terms malaria, tularemia, anthrax are used for the diseases caused by pathogens such as Plasmodium malariae, Francisella tularensis and Bacillus anthracis.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) The invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1, 3-5 and 8-11 are rejected under 35 U.S.C. 102(b) as being anticipated by O'Hagan Derek (Journal of Pharmacy and Pharmacology, Vol. 50, No. 1, pp.1-10, 1998). Prior art of record. USPTO 892, 12 /22/2003.

The claims are drawn a vaccine composition for inducing an immune response to a pathogen comprising a nucleic acid encoding an antigen in a biodegradable polymer.

O'Hagan Derek teaches a vaccine composition for inducing an immune response to a pathogen comprising a nucleic acid encoding an antigen in a biodegradable polymer (see abstract). O'Hagan teaches poly (lactide-co-glycolide) a biodegradable polymer (page 6). O'Hagan teaches a variety of pathogens including malaria and *Helicobacter pylori* (see pages 2 and 3). O'Hagan teaches encapsulation (page 6), adjuvants (page 5) particulates less than 5 micron and greater than 10 micron (see page 6). O'Hagan teaches mucosal immunization including nasal and oral (page 4). O'Hagan does not specifically teach that the composition is mucoadhesive. However, O'Hagan teaches that mucosal administration of the vaccine, which enhances the effectiveness of the vaccine (see abstract). O'Hagan teaches all the limitations of claimed invention. Limitations such as mucoadhesiveness of the formulation will be an inherent property of a microparticle formulated for mucosal delivery. O'Hagan does not explicitly teach an opened –celled polymeric foam of approximately 95% void volume or a particle thereof. Such limitation will be an inherent property of microparticle formulated for mucosal delivery taught by O'Hagan. Because the properties of O'Hagan composition and the claimed composition are the same baring evidence to the contrary. The prior teaches the claimed invention.

12. Claims 1, 3-5 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Perez et al. (Journal of Controlled Release, Vol. 75, pp.211-224, 2001). Prior art of record, Applicants' 1449, 10/31/2003.

The claims are drawn a vaccine composition for inducing an immune response to a pathogen comprising a nucleic acid encoding an antigen in a biodegradable polymer.

Perez et al. teach a vaccine composition for inducing an immune response to a pathogen comprising a nucleic acid encoding an antigen in a biodegradable polymer (see abstract). Perez et al. teach poly (lactide-co-glycolide) a biodegradable polymer (see abstract). Perez et al. teach plasmid DNA (see abstract). Perez et al. teach encapsulation (page 213), particulates less than 5 micron (see abstract). Perez et al. teach that the composition is mucoadhesive (see page 212). Perez et al. do not teach an opened –celled polymeric foam of approximately 95% void volume or a particle thereof. Such limitation will be an inherent property of microparticle formulated for mucosal delivery taught by Perez et al. Because the properties of Perez et al. composition and the claimed composition are the same baring evidence to the contrary. The prior teaches the claimed invention.

Status of the Claims

12. No claims allowed.

Claims 1, 3-11 stand rejected.

Conclusion

13. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Khatol Shahnan-Shah whose telephone number is (571)-272-0863. The examiner can normally be reached on Monday-Friday 7:30 AM-5:00 PM If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864.
The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Khatol Shahnan-Shah
B.S., Pharm, M.S.
Art Unit 1645
August 2, 2006

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER